

CLAIMS

What is claimed is:

- ✓ 1. A method for diagnosis of one or more single nucleotide polymorphism(s) in NK1R gene in a human, which method comprises determining the sequence of the nucleic acid of the human at one or more positions:
- 2361 in exon 1 as defined by the position in SEQ ID No. 1;
1371 in the promoter element as defined by the position in SEQ ID No.1;
271 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179;
10 272 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179;
245 in exon 5 as defined by the position in EMBL ACCESSION NO. X 65181;
461 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;
495 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;
600 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;
15 809 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;
and determining the status of the human by reference to polymorphism in NK1R.
2. A method according to claim 1 in which the single nucleotide polymorphism at position 2361 in exon 1 is presence of C and/or T, the single nucleotide polymorphism at position 1371 in the promoter element is presence of A and/or G, the single nucleotide polymorphism at position 271 near exon 3 is presence of G and/or T, the single nucleotide polymorphism at position 272 near exon 3 is presence of A and/or a single base deletion at this position, the single nucleotide polymorphism at position 245 in exon 5 is presence of C and/or a single base deletion at this position, the single nucleotide polymorphism at position 25 461 in the 3' UTR is presence of G and/or C, the single nucleotide polymorphism at position 495 in the 3' UTR is the presence of T and/or a single base insertion of A at this position, single nucleotide polymorphism at position 600 in the 3' UTR is presence of A and/or G, the single nucleotide polymorphism at position 809 in the 3' UTR is presence of C and/or T.
- 30 3. A method as claimed in claim 1 or 2, wherein the region containing the potential polymorphism is amplified by polymerase chain reaction prior to determining the sequence.

4. A method as claimed in any of claims 1 - 3, wherein the presence or absence of the polymorphism is detected by reference to the loss or gain of, optionally engineered, sites recognised by restriction enzymes.
5. A method according to claim 1 or claim 2, in which the sequence is determined by a method selected from ARMS-allele specific amplification, allele specific hybridisation, oligonucleotide ligation assay and restriction fragment length polymorphism (RFLP).
6. A method as claimed in any of the preceding claims for use in assessing the predisposition and/or susceptibility of an individual to diseases mediated by NK1R ligands.
- ✓ 7. A nucleic acid comprising any one of the following polymorphism containing sequences:
- the nucleic acid sequence of SEQ ID No. 1 with T at position 2361 in exon 1 as defined by the position in SEQ ID No. 1;
 - the nucleic acid sequence of EMBL ACCESSION NO. X 65179 with T at position 271 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179;
 - the nucleic acid sequence of EMBL ACCESSION NO. X 65179 with a single base deletion at position 272 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179;
 - the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with a single base deletion at position 245 in exon 5 as defined by the position in EMBL ACCESSION NO. X 65181;
 - the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with C at position 461 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181;
 - the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with A inserted at position 495 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181;
 - the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with G at position 600 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181;
 - the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with T at position 809 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181;
 - the nucleic acid sequence of SEQ ID No. 1 with G at position 1371 in the promoter element as defined by the position in SEQ ID No. 1;

or a complementary strand thereof or a fragment thereof of at least 20 bases comprising at least one of the polymorphisms.

- ✓ 8. A diagnostic nucleic acid primer capable of detecting a polymorphism in the NK1R gene at one or more of positions: 2361 in exon 1 as defined by the position SEQ ID No. 1; 1371 in the promoter element as defined by the position SEQ ID No. 1; 271 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179; 272 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179; 245 in exon 5 as defined by the position in EMBL ACCESSION NO. X 65181; 461 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181; 495 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181; 600 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181; 809 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181, in the NR1R gene.
- 15 9. A diagnostic primer as claimed in claim 8 which is an allele specific primer adapted for use in ARMS.
- ✓ 10. An allele-specific oligonucleotide probe capable of detecting a polymorphism in the NK1R gene at one or more of positions: 2361 in exon 1 as defined by the position in SEQ ID No. 1; 1371 in the promoter element as defined by the position in SEQ ID No. 1; 271 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179; 272 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179; 245 in exon 5 as defined by the position in EMBL ACCESSION NO. X 65181; 461 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181; 495 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181; 600 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181; 809 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181, in the NR1R gene.
- 25 11. A diagnostic kit comprising one or more diagnostic primer(s) as defined in claim 8 or 9 and/or one or more allele-specific oligonucleotide probes(s) as defined in claim 10.

✓ 12. An allelic variant of human NK1R polypeptide having a C-terminal deletion of 26 amino acids.

✓ 13. A method of treating a human in need of treatment with an NK1R ligand antagonist
5 drug in which the method comprises:

(i) diagnosis of a single nucleotide polymorphism in the NK1R gene in the human, which diagnosis comprises determining the sequence of nucleic acid at one of more of positions:

2361 in exon 1 as defined by the position SEQ ID No. 1;

1371 in the promoter element as defined by the position in SEQ ID No. 1;

10 271 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179;

272 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179;

245 in exon 5 as defined by the position in EMBL ACCESSION NO. X 65181;

461 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;

495 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;

15 600 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;

809 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;

and determining the status of the human by reference to polymorphism in the NK1R gene;

and

(ii) administering an effective amount of a NK1R ligand antagonist.

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✓ 14. Use of an NK1R ligand antagonist drug in preparation of a medicament for treating a NK1R ligand mediated disease, particularly asthma, in a human diagnosed as having a single nucleotide polymorphism at one or more of positions:

2361 in exon 1 as defined by the position in SEQ ID No. 1;

25 1371 in the promoter element as defined by the position in SEQ ID No. 1;

271 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179;

272 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179;

245 in exon 5 as defined by the position in EMBL ACCESSION NO. X 65181;

461 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;

30 495 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;

600 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;

809 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181.

- ✓ 15. A pharmaceutical pack comprising an NK1R antagonist drug and instructions for administration of the drug to humans diagnostically tested for a single nucleotide polymorphism at one or more positions:
2361 in exon 1 as defined by the position in SEQ ID No. 1;
5 1371 in the promoter element as defined by the position in SEQ ID No. 1;
271 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179;
272 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179;
245 in exon 5 as defined by the position in EMBL ACCESSION NO. X 65181;
461 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;
10 495 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;
600 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181;
809 in the 3' UTR as defined by the position in EMBL ACCESSION NO. X65181.
- ✓ 16. A computer readable medium having stored thereon a member selected from the group
15 consisting of: a nucleic acid comprising SEQ ID No. 1; a set of nucleic acids wherein at least one of said sequences comprises SEQ ID No. 1; a data set representing a nucleic acid sequence comprising SEQ ID No. 1; a nucleic acid consisting of SEQ ID No. 1; a set of nucleic acids wherein at least one of said sequences consists of the sequence of SEQ ID No. 1; a nucleic acid comprising any part of a sequence selected from the group consisting of: SEQ
20 ID No. 1, EMBL ACCESSION NO. X 65177, EMBL ACCESSION NO. X 65179, EMBL ACCESSION NO. X 65179 or EMBL ACCESSION NO. X 65181, which part includes at least one of the polymorphisms identified in claim 1.
- ✓ 17. A method for performing sequence identification, said method comprising the steps of
25 providing a nucleic acid sequence comprising a sequence selected from the group consisting of: the nucleic acid sequence of SEQ ID No. 1 with T at position 2361 in exon 1 as defined by the position in SEQ ID No. 1; the nucleic acid sequence of EMBL ACCESSION NO. X 65179 with T at position 271 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179; the nucleic acid sequence of EMBL ACCESSION NO. X 65179 with a single
30 base deletion at position 272 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179; the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with a single base deletion at position 245 in exon 5 as defined by the position in EMBL ACCESSION NO.

X 65181; the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with C at position 461 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181; the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with A inserted at position 495 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181; the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with G at position 600 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181; the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with T at position 809 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181; the nucleic acid sequence of SEQ ID No. 1 with G at position 1371 in the promoter element as defined by the position in SEQ ID No. 1; or a complementary strand thereof or a fragment thereof of at least 20 bases comprising at least one of the polymorphisms; and comparing said nucleic acid sequence to at least one other nucleic acid or polypeptide sequence to identify identity.

18. A method for performing sequence identification, said method comprising the steps of providing one or more of the following polymorphism containing nucleic acid sequences: the nucleic acid sequence of SEQ ID No. 1 with T at position 2361 in exon 1 as defined by the position in SEQ ID No. 1; the nucleic acid sequence of EMBL ACCESSION NO. X 65179 with T at position 271 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179; the nucleic acid sequence of EMBL ACCESSION NO. X 65179 with a single base deletion at position 272 near exon 3 as defined by the position in EMBL ACCESSION NO. X 65179; the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with a single base deletion at position 245 in exon 5 as defined by the position in EMBL ACCESSION NO. X 65181; the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with C at position 461 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181; the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with A inserted at position 495 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181; the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with G at position 600 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181; the nucleic acid sequence of EMBL ACCESSION NO. X 65181 with T at position 809 in the 3'UTR as defined by the position in EMBL ACCESSION NO. X 65181; the nucleic acid sequence of SEQ ID No. 1 with G at position 1371 in the promoter element as defined by the position in SEQ ID No. 1; or a complementary strand thereof or a fragment thereof of at least 20 bases comprising at

least one of the polymorphisms, in a computer readable medium; and comparing said nucleic acid sequence to at least one other nucleic acid or polypeptide sequence to determine identity.

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